

# I. Remarks

Claims 128, 131, 135-137, 147-148, and 151-155 are pending in the application. Claims 129-130, 146, and 156-157 were previously canceled. A Declaration under 37 CFR §1.132 and two (2) Terminal Disclaimers (PTO/SB/26(09-04) along with the requisite fees accompanies this Response.

## II. Rejection under 35 USC §103(a)

Examiner has rejected Claims 128, 135-136, and 147-148 under Section 103(a) as being obvious to one skilled in the art over the disclosure of Kaufman et al (USPN 5,770,585) on the grounds that Kaufman *et al* teaches:

*"a method of treating lung cancer (respiratory cancer) comprising delivering a liquid dispersion (aerosol liquid) or breathable gas (inhalation) containing an anthracycline such as doxorubicin to the lungs"; and*

*"Kaufman clearly states that his drug composition can be delivered to the lungs as a breathable (inhalation) gas (aerosol)."*

To facilitate the discussion that follows, Claims 11 and 12 of Kaufman and Claim 128 of the above-identified invention are compared in below.

Kaufman	USSN 10/066,831
11. A method of delivering a drug to the lung of an animal comprising the step of: administering a stable homogeneous, water-in-perfluorochemical liquid dispersion to the animal lung or a section thereof, said dispersion comprising a perfluorochemical liquid, water, surfactant and drug, said perfluorochemical constituting greater than 50% by volume of said dispersion, said drug contained in said dispersion in an effective therapeutic amount.	128. A method of treating cancer of the respiratory tract in a patient in need of treatment which comprises administering by inhalation a pharmaceutically safe and effective amount of an aerosolized vesicant agent; wherein said vesicant anti-cancer agent is unencapsulated and wherein the particle size of said aerosol is from about 0.1 µm to about 10.0 µm.
12. The method of claim 11 further comprising the step of delivering a breathable gas to the lung with a mechanical ventilator during said administration.	

When Claim 11 of Kaufman is compared to Claim 128 of the present invention, it is clear that the method taught by Kaufman is unequivocally different from the method claimed herein. Contrary to Examiner's assertion, Kaufman does not deliver a drug to the lungs of a patient in the form of an aerosol. Kaufman teaches the "administration" of a water-in-perfluorocarbon liquid dispersion directly to the lungs. The liquid dispersion is placed in the lung (i.e. administered) using an endotracheal tube. In contrast, in the practice of the method claimed

herein, an aerosol of fine droplets containing the drug is inhaled into the lungs by the patient being treated.

Claim 12 of Kaufman provides that a "breathable gas" may be administered to the lung of a patient using a mechanical ventilator in addition to the administration of the liquid perfluorocarbon dispersion. The breathable gas referred to by Kaufman is air or oxygen and is administered to the patient using a conventional gas ventilator.

In the practice of the method claimed herein the vesicant anticancer agent is either dissolved or suspended in a liquid or gas and then aerosolized to produce aerosol particles ranging from about 0.1  $\mu\text{m}$  to about 10.0  $\mu\text{m}$  in diameter. The aerosol is produced using conventional aerosolization means known in the art, e.g., a nebulizer, inhaler, metered dose inhaler or electrostatic aerosolization means. The patient inhales the aerosol droplets into her lungs when practicing the method of the invention claimed herein. In contrast, in the practice of the method described by Kaufman, a nurse, doctor or respiratory therapist must place the liquid perfluorocarbon dispersions into the lungs of the patients using an endotracheal tube.

Despite Applicants arguments relying on specific text in the Kaufman specification which distinguishes the Kaufman method from a method of administration using an aerosol (see p. 7 of the Submission with Request for Continued Examination dated 12/16/2004), Examiner continues to assert that Kaufman teaches the administration of an aerosolized drug but offers no evidence to support his belief.

Attached is the Declaration of James N. Allen, Jr., MD. As can be seen from Dr. Allen's *Curriculum vitae*, Dr. Allen has a high degree of skill in the art of treating patients with respiratory diseases such as lung cancer. As stated in the attached Declaration, Dr. Allen has read the Kaufman reference and he declares the following:

"In my opinion, the Kaufman patent does not describe a method of administering the liquid perfluorocarbon emulsion of the Kaufman invention to the lungs of an animal in the form of an aerosol."

Dr. Allen goes on to state that:

"Based on my training and experience, the method detailed by the protocol of Kaufman is commonly referred to as partial liquid ventilation (PLV). Partial liquid ventilation involves filling the lungs of a patient with a liquid perfluorocarbon usually, perflubron. The liquid may be placed in the lungs via an endotracheal tube and thereafter the patient is connected to a conventional gas ventilator or the perfluorocarbon liquid is trickled into the lungs of a patient connected to a ventilator through a side-port on the endotracheal tube connecting the patient to the ventilator"

It is clear from the Allen Declaration that Dr. Allen, one who is indisputably highly skilled in this art, does not read the Kaufman reference to teach or suggest the administration of the liquid perfluorocarbon emulsion of the Kaufman invention to a patient in the form of an aerosol.

It is respectfully submitted that the Examiner may not substitute his unsubstantiated opinion that the Kaufman reference teaches the administration of a drug in the form of an aerosol for the analysis and opinion of one skilled in this art which is based upon education and experience actually treating patients with lung diseases. Accordingly, the rejection of Claims

128, 135-136, and 147-148 under 35 USC §103(a) as being obvious over the Kaufman reference has been overcome.

### III. "Obviousness" Type Double Patenting Rejection

Examiner rejects Applicants' claims for double patenting over two issued patents: USPN 6,384,209 and USPN 6,419,901.

USPN 6,384,209 and USPN 6,419,901 are commonly owned by Zivena, Inc. who is also the record owner of the above-identified application. Enclosed herewith are two (2) Terminal Disclaimers both in accordance with 37 CFR §1.321(c), disclaiming the term of the patent which may issue from the above-identified application over the term of USPN 6419901 and USPN 6348209. It is believed that the filing of these disclaimers effectively overcomes Examiner's rejection of Applicants' pending claims on the basis of "obviousness" type double patenting.

### IV. Conclusion

Based on the arguments made herein and on the Declaration of Dr. James N. Allen, Jr., it is respectfully asserted that Examiner's rejection of the claims under 35 USC §103(a) has been overcome and that the Obviousness Type Double Patenting rejection has been obviated by the filing of the Terminal Disclaimers accompanying this Response. Accordingly, it is respectfully asserted that this application is in condition for allowance; Examiner is respectfully requested to withdraw all rejections and to issue a Notice of Allowance.

Respectfully submitted,

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